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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/080,767	02/22/2002	Glen H. Erikson	E1047/20075	2939

3000 7590 03/17/2003

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WILDER, CYNTHIA B	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 03/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/080,767	Applicant(s) Ericken et al.
	Examiner Cynthia B Wilder	Art Unit 1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 18, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-47* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

1.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his invention.

2. Claims 1-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claims 1-47 are indefinite for the recitation of "conjugated" because the term has not been defined in the specification, the terminology does not have a common meaning in the art, and it cannot be determine what is encompassed by "conjugated" in the context of the claimed invention. It is unclear if "conjugate" refer to a covalent attachment or attachment via ionic bonds or attachment via van der Waals attractions or attachment via electrostatic interaction or etc. Accordingly, clarification is required with respect to what constitutes "conjugation" in the context of the claimed invention.

(b) Claims 7 and 8 are indefinite at the recitation of "free nucleobase" because the term has not been clearly defined in the specification and it cannot be determined what constitutes a free nucleobase. For example, does "free nucleobase" means that an extra nucleobase is added to the blocking agent, or does it mean that the nucleobase is different or distinct from the nucleobases of the target and/or probe, or does the term "free nucleobase" means that the base is incapable of base-

pairing or hybridizing to the target and/or probe? Additionally, if the "free nucleobase" is to be interpreted as an extra base, how can the free nucleobase be the only nucleobase of the blocking agent? Clarification is required as to what constitutes a "free nucleobase" in the context of the claimed invention.

(c) Claims 10-17 are confusing at the recitation of "wherein at least one nucleobase is provided in a quantity that is 1-200% of a number of the probe or number of the target nucleobase" because it cannot be determined if reference is being made to a molar concentration or if reference is being made to a length limitation of the nucleobases or if reference is being made to the amount of nucleobases capable of complementarity between the nucleobases of the blocking agent, probe and target. Clarification is required as to what is meant by "a quantity of at least one nucleobase".

(d) Claim 25 lacks antecedent basis for "said group" because claim 1 from which it depends does not recite any groups. It is suggested changing "said" to "the" such that the claim reads "selected from the group consisting of.." for proper Markush language.

Claim Rejections - 35 USC § 102(b)

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The specification defines "blocking agent"as preferably a single naturally-occurring nucleobase selected from the group consisting of A, T, C, G and U, other naturally occurring bases or a synthetic nucleobase analogue. The specification states that the "blocking agent" is preferably provided in the form of a free base, a nucleoside or a nucleotide" and functions to enhances nucleic acid binding by conjugating to a probe and/or target nucleic acid, thus mitigating the consequences of hairpin formation (specification, page 4, 4th paragraph). For the purposes of application of prior art, the instant invention has been given the broadest, reasonable interpretation of the claim limitations. Accordingly, the claimed limitation "blocking agent" has been interpreted as any nucleic acid sequence that binds to a portion of RNA or DNA and thus imposes an altered secondary or tertiary structure on the targeted region of the nucleic acid.

4. Claims 1-5, 18-22, 24-26, 28-32, 34, 41, 42, 45 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Hogan et al. (US 5,030,557, July 9, 1991). Regarding claim 1, Hogan et al. teach a method of forming a complex between a probe containing probe nucleobases and a target containing target nucleobases, comprising mixing said probe and said target under hybridizing conditions, wherein at least one blocking agent (helper oligonucleotide) comprising at least one nucleobase is conjugated to said target nucleobase prior to hybridizing said probe to said target and wherein said conjugation enhances an avidity and/or specificity of said hybridizing (see abstract and col. 4, lines 19-44 and col. 5, beginning at line 64 to col. 6, line 4). Therefore, the reference of Hogan et al. meets all of the claimed limitations of claim 1.

Regarding claim 2, Hogan et al. teach the method of claim 1, wherein said conjugation enhances said avidity and/or specificity by hindering said probe and/or target from existing in a conformation antithetical to said hybridization (see abstract and col. 4, lines 39-36; see also Figure 3).

Regarding claim 3, Hogan et al. teach the method of claim wherein said conformation is a hairpin structure (see figure 3).

Regarding claims 4 and 5, Hogan et al. teach the method of claim 1, wherein the blocking agent is not greater than about 50 nucleobases, which is interpreted as the blocking agent comprising up to 50 nucleobases (col. 5, lines 64-65).

Regarding claim 18, Hogan et al. teach the method of claim 1, wherein said probe nucleobases are arranged in a probe sequence of interspersed purines and pyrimidines (see col. 8, Ex. 1, lines 20-24, sequences for "Helper A" and "Helper B"). Hogan et al. further teach that the probe may comprise one or more nucleotides not complementary to the corresponding bases in the target sequence (col. 5, lines 49-52; see also col. 6, lines 65-68).

Regarding claims 19 and 20, Hogan et al. teach that the nucleotide (base + sugar + phosphate: col. 5, lines 21-24) probe is an oligonucleotide or polynucleotide and may be an analogue of the phosphate ester structure of a typical DNA or RNA. Hogan et al. states that for example, the probe may have an alkyl or phosphate, a phosphoraothioate or other modified backbone structure (col. 5, lines 44-55, 59-63). The charge of the nucleotide probe as claimed in claim 20 is inherent in

teachings of Hogan et al. of the modified backbone structures which may cause the probe to be uncharged or positively charged.

Regarding claims 21 and 22, Hogan et al. teach the method of claim 1, wherein the target is is a property conferred by the base sequence of a single strand of DNA or RNA which, with another DNA or RNA strand, may form a hybrid of double stranded DNA:DNA, RNA:RNA or DNA:RNA (col. 5, lines 32-38).

Regarding claim 24, Hogan et al. teach the method of claim 1, wherein said at least one blocking agent is not conjugated to said probe (see abstract and col. 4, lines 31-33).

Regarding claim 25, Hogan et al. teach the method of claim 1, wherein said at least one blocking agent comprises nucleobases of DNA and RNA (col. 7, lines 28-33) which are selected from the group consisting of adenine (A), thymine (T), Uracil (U), guanine (G) or cytosine (c) (see also col. 5, lines 32-41).

Regarding claim 26, Hogan et al. teach the method of claim 1, wherein said at least one blocking agent is a synthetic nucleobase analogue (col. 7, lines 34-35).

Regarding claim 28, Hogan et al. teach the method of claim 1, wherein said probe has a probe directionality anti-parallel to a target strand directionality of said target (col. 6, lines 61-64).

Regarding claim 29, Hogan et al. teach a method of claim 1, wherein the probe is further labeled for detection of the complex (see col. 5, lines 54-59 and Example 1, specifically col. 8, lines 25-63).

Regarding claim 30, Hogan et al. teach the method of claim 29, wherein said complex is capable of being formed when the target DNA is bound to a solid surface (col. 14, 5-8).

Regarding claims 31 and 32, Hogan et al. teach the method of claim 29, wherein said complex is detected by a change in a signal associated with a label wherein the label is a radioisotope (see examples 1 and 2). Hogan et al. further teach wherein the probe can be labeled with any suitable label such as a radioisotope, or an enzyme such as horseradish peroxidase or alkaline phosphatase which catalyzes a color forming reaction of a suitable substrate, or the label may be a fluoremetric moiety such as acridinium ester (col. 14, lines 26-34).

Regarding claim 34, Hogan et al. teach the method of claim 29, wherein said detecting is conducted in a tested medium under a varied condition wherein said varied condition is a change in a temperature of a said test medium (col. 14, lines 42-46).

Regarding claim 41, Hogan et al. teach the method of claim 29, wherein a kit is provided for detecting a target nucleic acid. the kit comprises the blocking agent, labeled probe and also includes positive and negative controls and standards for obtaining quantitative results (col. 14, lines 47-54). Therefore, Hogan et al. suggest that the target can be quantitated.

Regarding claim 42, Hogan et al. teach the method of claim 29, wherein an extend of complementarity between the probe and said target is detected (col. 7, lines 19-22).

Regarding claim 45, Hogan et al. teach the method of claim 1, wherein the probe and the target hybridize in accordance with a Watson-Crick motif to form duplex and triplex complexes (see Figures 1-3 and col. 5, lines 32-49, 64-68 and col. 6, lines 1-4).

Regarding claim 47, Hogan et al. teach the method of claim 1, wherein said hybridizing may be conducted in a homogeneous medium (col. 14, lines 18-21). Therefore, Hogan et al. also meet all of the limitations of claims 2-5, 18-22, 24-26, 28-32, 34, 41, 42, 45 and 47 of the instant invention.

Claim Rejections - 35 USC § 102(e)

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the Applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

For the purposes of application of prior art, the instant invention has been given the broadest, reasonable interpretation of the claim limitations. Accordingly, the claimed limitation "blocking agent" has been interpreted as any nucleic acid molecule, including a modified nucleic acid molecule, that binds to a portion of RNA or DNA and thus imposes an altered structure on the targeted region of the nucleic acid.

6. Claims 1, 23, 27, 43-44, 46 rejected under 35 U.S.C. 102(e) as being anticipated by Meyer, Jr, et al (6,312,925 B1, effective filing date May 8, 1997). Regarding claim 1, Meyer, Jr. et al. teach a method of forming a complex between a probe containing nucleobase and a target containing target nucleobase, comprising mixing said probe and said target under hybridizing conditions, wherein at least one blocking agent (modifying agent) comprising at least one nucleobase is conjugated to said probe and/or target, wherein said conjugation inducing a heritable change in the target sequence thus forming a new oligonucleotide-DNA hybrid with greater stability than the original-DNA-DNA duplex (Abstract, col. 7, lines 32, 33, 35 and column 12, lines 45-48, 66-67 to col. 13, lines 1-4).

Regarding claim 23, Meyer Jr et al. teach the method of claim 1, wherein said at least one blocking agent is not conjugated to said target (col. 4, lines 6-18).

Regarding claim 27, Meyer Jr. et al. teach the method of claim 1, wherein said probe has a probe directionality parallel to a target strand directionality of said target (col. 6, lines 67 to col. 7, lines 18).

Regarding claim 43, Meyer Jr. et al. teach the method of claim 1, wherein formation of said complex is facilitated by at least one intercalator (col. 6, lines 47-53).

Regarding claim 44, Meyer Jr. et al. teach the method of claim 1, wherein said complex is formed in a presence of at least one other probe containing a sequence of nucleobase complementary to a secondary target sequence different from a primary target sequence of said target; said other probe differs from said probe by only a single nucleobase ([oligonucleotide composition comprising modifying agent], col. 6, lines 49-55), said other probe form a complex with said target and said

target is detected (abstract and col. 9, lines 39-51; col. 10, lines 20-50; col. 11, lines 66-67 to col. 12, lines 22, 43-48).

Regarding claim 46, Meyer Jr, et al. teach the method of claim 1, wherein the probe and the target hybridize in accordance with a homologous binding motif to form a triplex nucleic acid complex (col. 7, line 6-11).

Therefore, Meyer Jr. et al. meets all of the claimed limitations of claims 1, 23, 27, 43-44, 46 of the instant invention.

7. Claims 1, 4, 5, 29-31, 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Becker et al. (6,130,038, effective filing date, July 1996). Regarding claim 1, Becker et al. teach a method of forming a complex, said method comprising mixing a probe containing probe nucleobase with a target containing target nucleobase under hybridizing conditions, wherein at least one blocking agent (modifying agent) comprising at least one nucleobase is conjugated to said probe and/or said target prior to hybridizing said probe with said target, wherein said conjugation enhances avidity and specificity of said hybridizing (col. 9, lines 42-67 to col. 10, lines 1-25).

Regarding claim 4, Becker et al. teach the method of claim 1, wherein said at least one blocking agent contains up to five nucleobases (col. 8, lines 53-63 and col. 21, lines 42-48).

Regarding claim 5, Becker et al. teach the method of claim 1, wherein said at least one blocking agent contains up to two nucleobases (col. 8, lines 53-59).

Regarding claim 29, Becker et al. teach the method of claim 1, further comprising detecting said complex (col. 11, lines 28-46; col. 12, lines 8-26 and col. 22, lines 46-47).

Regarding claim 30, Becker et al. teach the method of claim 1, wherein said complex is formed with at said target is bound to a substrate (col. 12, lines 12-17).

Regarding claim 31, Becker et al. teach the method of claim 29, wherein said complex is detected by a change in a signal associated with a label (col. 2, lines 44-53)

Regarding claim 39, Becker et al. teach the method of claim 31, wherein said label is added free in solution to said test medium such that it is capable of binding to the desired nucleic acid (col. col. 3, lines 35-40 and 12, lines 56-67).

Therefore, Becker et al. meets all of the claimed limitations of claims 1, 4, 5, 29-31, 39 of the instant invention.

Claim Rejections - 35 USC § 103(a)

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made

in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 32-34, 36-38, 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hogan et al. as previously applied above in view of (Heller et al. 6,048,690, May 1997). Regarding claims 32-33, Hogan et al. teach a method of forming a complex between a probe containing probe nucleobases and a target containing target nucleobases, comprising mixing said probe and said target under hybridizing conditions, wherein at least one blocking agent (helper oligonucleotide) comprising at least one nucleobase is conjugated to said target nucleobase prior to hybridizing said probe to said target and wherein said conjugation enhances an avidity and/or specificity of said hybridizing.

The method of Hogan et al. differs from that of the claimed invention in that Hogan et al. do not teach wherein in said method the complex is detected by analyzing an electronic characteristic of said complex.

Heller et al. teach a method for hybridization analysis by analyzing an electronic characteristic of the hybridization sample (abstract and col. 1, lines 44-55). Heller et al. teach wherein the method comprises providing a target comprising at least one nucleic acid sequence; providing a probe comprising a nucleic acid sequence; mixing the probe and the target to a hybridization medium to provide a complex, adding to the complex a label wherein said label is an environmental sensitive emission label such as a chromophore or fluorophore or luminescent molecule or moiety or metal chelate or enzyme or peptide or amino acid (col. 6, lines 57059);

subjecting the hybridization product and label to a varying elelctrophorectic force, monitoring the emission from the label and analyzing the monitored emission to determine the electronic fluorescent perturbation effect (abstract and col. 5, lines 59-6- 67 to col. 6, lines 1-9) which is a rise or spike in fluorescent intensity prior to dehybridization of a fluorescent labeled probe from a capture sequence attached to a microlocation test tube (col. 4, lines 62-66). Heller et al. further teach that this method is a powerful analytical tool for DNA hybridization analysis, particularly for the near instantaneous, e.g., less than one minute, and especially less than 5 seconds, discrimination of match/mismatched DNA hybrids and is also useful for novel DNA sequencing applications (col. 5, lines 16-21).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to have modified the method of forming a complex as taught by Hogan et al. to encompass detection of the complex by analyzing an electronic characteristic as taught by Heller et al. One of ordinary skill in the art would have been motivated to do so for the advantages taught by Heller et al. that a method, such as a fluorescent perturbation effect, which utilizes electronic power(current and voltage) as described is a powerful tool for DNA hybridization analysis, particularly for the near instantaneous, e.g., less than one minute, and especially less than 5 seconds, discrimination of match/mismatched DNA hybrids and is also useful for novel DNA sequencing applications.

Regarding claim 34, Heller et al. teach the method of claim 29, wherein the method of detecting is conducted in a test medium under a varied condition, wherein said varied condition is

a change in an electric current and change in an electrical property (col. 7, lines 14-16 and col. 10, lines 63-67 to col. 11, line 10, see also Example 3).

Regarding claim 36, Heller et al. teach the method of claim 29, wherein said electrical property is electrical conductance (col. 10, lines 63-65).

Regarding claim 37, Heller et al. teach the method of claim 34, wherein said electrical property is amplitude of a signal propagated in said transmission line in said test medium (col. 9, lines 1-6).

Regarding claim 38, Heller et al. teach the method of claim 34, wherein said complex is detected under serially varied conditions ((col. 7, lines 14-16 and col. 10, lines 63-67 to col. 11, line 10, see also Example 3).

Regarding claim 40, Heller et al. teach the method of claim 29, further comprising detecting a signal from a label wherein said signal is correlated to a binding affinity between said probe and said target; varying conditions of a test medium and detecting a subsequent signal and comparing the first signal and subsequent signal (See examples 3 and 4).

10. Claims 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hogan et al. as previously applied above in view of Wu et al. (5,846,729, filing date July 1, 1997). Regarding claims 35, Hogan et al. teach a method of forming a complex between a probe containing probe nucleobases and a target containing target nucleobases, comprising mixing said probe and said target under hybridizing conditions, wherein at least one blocking agent (helper oligonucleotide) comprising at least one nucleobase is conjugated to said target nucleobase prior to hybridizing said

probe to said target and wherein said conjugation enhances an avidity and/or specificity of said hybridizing.

The method of Hogan et al. differs from that of the claimed invention in that Hogan et al. do not teach wherein in said method the complex is detected in a test medium under varied conditions wherein said varied condition is a change in a number of photons in the test medium. Hogan et al. additionally do not teach wherein a laser beam is applied to said test medium to effect said change in the number of photons.

Wu et al. teach a method of forming a hybridization complex between a target nucleic acid and probe in a test a medium and detecting said hybridization complex by applying a laser beam to the hybridization sample which is capable of effecting changes in the number of photons and measuring signal intensity (col. 3, lines 29-44, col. 5, lines 57-58, col. 6, lines 5-51). Wu et al. teaches that by using this method for detecting hybridization, no separation of the hybridization complex from the uncomplexed probes is necessary prior to signal determination (col. 6, lines 52-54). Wu et al. teach that additionally nucleotide sequence information can be determined by monitoring a change in the overall signal intensity, which is a function of hybridization and hybridization efficiency (col. 6, lines 62-65).

Therefore, in view of the foregoing, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have been motivated to have modified the method of detecting a hybridization complex as taught by Hogan et al. to encompass detection of the complex by applying a laser beam capable of effecting changes in the number of photons in a test medium

as taught by Wu et al. One of ordinary skill in the art would have been motivated to do so for the advantage taught by Wu et al. that the method, wherein a laser beam is applied to detect a hybridization complex, requires no separation of unhybridized probes from the hybridization complex prior to signal detection and for the advantage that sequence information can be determined by monitoring a change in the overall signal intensity which is a function of hybridization and hybridization efficiency.

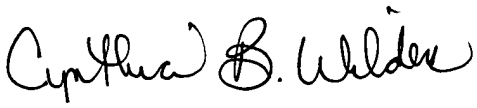
Conclusion

11. No claims are allowed. However, claim 6 and claims depending therefrom (claims 7-17) are free of the prior art. No prior art was found teaching a method of forming a complex containing a probe nucleobase and target nucleobase under hybridizing conditions, wherein at least one blocking agent is conjugated to at least one probe and/or said target prior to said hybridizing of said probe with said target and wherein said at least one nucleobase is the only nucleobase contained in said at least one blocking agent. No motivation could be found in the prior art for said limitation. Accordingly, an obviousness-type rejection could not be made.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The examiner can normally be reached on Monday through Thursday from 9:30 am to 6:30 pm and on Friday from 9:30 am to 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. The official fax phone number for the Group is (703) 308-4242. The unofficial fax number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Group's receptionist at (703) 308-0196.



cbw
March 11, 2003

Cynthia B. Wilder, Ph.D.
Patent Examiner
Art Unit 1637